### **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:
A61K 47/48

A2 (11) International Publication Number: WO 99/04820
(43) International Publication Date: 4 February 1999 (04.02.99)

(21) International Application Number: PCT/EP98/04219

(22) International Filing Date: 2 July 1998 (02.07.98)

(30) Priority Data:

60/053,211 21 July 1997 (21.07.97) US 9704170-1 14 November 1997 (14.11.97) SE

(71) Applicant (for all designated States except US): PHARMACIA & UPJOHN AB [SE/SE]; S-112 87 Stockholm (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SOEGAARD, Morten [DK/DK]; Rysensteensgade 16, DK-1564 Kopenhamn (DK). ABRAHMSEN; Lars [SE/SE]; Lillangsgatan 28, S-168 58 Bromma (SE). LANDO, Peter [SE/SE]; Carl Gustavs vag 26 A, S-211 46 Malmo (SE). FORSBERG, Göran [SE/SE]; Kulgranden 15A, S-226 49 Lund (SE). KALLAND, Terje [NO/SE]; Domberrevagen 4, S-246 32 Leddekopinge (SE). DOHLSTEN, Mikael [SE/SE]; Gerdagatan 12B, S-223 62 Lund (SE).

(74) Agent: MAZZINI, Giuseppe; Pharmacia & Upjohn S.p.A., Viale Pasteur, 10, I-20014 Nerviano (IT).

(81) Designated States: AU, BG, BR, CA, CN, CZ, HU, ID, IL, JP, KR, MX, NO, NZ, PL, RO, SG, SI, UA, US, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

#### **Published**

Without international search report and to be republished upon receipt of that report.

(54) Title: DIRECTED CYTOLYSIS OF TARGET CELLS, AGENTS AND COMPOSITIONS CAUSING CYTOLYSIS, AND COMPOUNDS THAT CAN BE USED TO PRODUCE THE AGENTS

#### (57) Abstract

A method for inactivating target cells in the presence of T cells by bringing the two types of cells in contact with a superantigen (SAG) in the presence of an immune modulator, characterized in that at least one of the superantigen and the immune modulator is in the form of a conjugate between a "free" superantigen (Sag) and a moiety targeting the conjugate to the target cells. A superantigen conjugate complying with the formula (I):  $(T)_x(Sag)_y(IM)_z$ ; a) T is a targeting moiety, Sag corresponds to a free superantigen, IM is an immune modulator that is not a superantigen and T, Sag and IM are linked together via organic linkers B; b) x, y and z are integers that typically are selected among 0–10 and represent the number of moieties T, Sag and IM, respetively, in a given conjugate molecule, with the provision that y > 0 and also one or both of x and z > 0. The superantigen conjugate is preferably a triple fusion protein. A targeted immune modulator, characterized in that it is a conjugate between a targeting moiety (T''') and a modified immune modulator (IM'''). The conjugate complies with a formula analogous to formula (I) except for the imperative presence of the modified immune modulator. A superantigen moiety may be present. A DNA molecule encoding a superantigen and an immune modulator.

# FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
ΑT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	ТJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
ВJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		